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REPORT

Pharmacoeconomics: friend or foe?

M Drummond

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The financial constraints faced by most health systems today make it necessary for manufacturers of new, expensive drugs to demonstrate value for money. This paper describes the different types of economic evaluation; the increasing use of these analysis in decision making; their application to new drugs in the field of rheumatoid arthritis; and the pros and cons of pharmacoeconomics studies from the perspective of the patients, the physicians, and the general population.

Given the limitations on healthcare resources, there is increased interest in assessing the value for money, or economic efficiency, of healthcare treatments and programmes. This is achieved through *economic evaluation*, in which the costs and consequences of alternative treatment strategies are compared.¹ When economic evaluation is applied to pharmaceuticals, such studies often go under the term “pharmacoeconomics”. This article describes the basic forms of economic evaluation, outlines the increasing formal requirement for such studies; discusses their application to new drugs in the field of rheumatoid arthritis; and assesses whether, on balance, the increased interest in economic analysis is favourable or unfavourable to patients, their physicians, and society at large.

WHAT IS PHARMACOECONOMICS?

The basic components of economic evaluation are shown in figure 1. In this example a new drug is being compared with existing practice, which could be an older drug, a non-pharmacological intervention or, in the case of a “break-through” drug, no active therapy.

In considering the costs and consequences, the two treatments themselves will have acquisition costs, but the economic costs and consequences will be much broader. For example, if the new drug is more efficacious than current therapy, there may be savings in other healthcare costs, such as hospitalisations. Alternatively, if the new drug has a better side effect profile, fewer drugs and procedures will be consumed in dealing with adverse events.

As the comparison of treatments, in an economic evaluation, requires data on efficacy, the economic study usually

builds on clinical assessments obtained from clinical trials. Sometimes economic evaluations are conducted alongside, or concurrently with, a given clinical trial. These are called *trial based* studies. However, economic evaluations are often undertaken based on a synthesis of data from a range of sources. If, in addition, they make use of decision-analytic or epidemiological models, they are called *modelling* studies. An important methodological feature of these studies is whether the assessments of clinical efficacy used in the model come from a systematic review of the relevant clinical literature. If the clinical data used in the economic evaluation do not accurately reflect the clinical evidence as a whole, the results of the economic study may be biased. Finally, the consideration of costs in figure 1 was restricted to healthcare costs. However, some economic evaluations adopt a broader, societal, perspective and consider costs falling on other government budgets, the patient and their family, or the broader economy, through patients or their carers being able to return to work if the treatment is sufficiently successful.

In situations where the two treatment options being considered are identical from a clinical perspective (for example, a comparison of a generic drug with a branded version of the same compound), the economic evaluation reduces to a comparison of costs only. However, such instances are quite rare and usually the difference in costs needs to be compared with an appropriate measure of the difference in consequences.

There are three main forms of economic evaluation. In the first form, *cost-effectiveness analysis* (CEA), the consequences are measured in the most obvious natural units of *effects*. The choice of units of measurement depends on the clinical field being studied. For example, in life-saving therapy, such as treatments for chronic renal failure, the most appropriate effectiveness measure would be years of life gained. On the other hand, in a field such as asthma, the most appropriate measure may be “asthma-free days” or “symptom-free days”. However, such studies leave us with important issues of interpretation. For example, if one drug is superior in some measures of outcome and inferior in others, how would one outcome be valued relative to another? One way around this would be to turn the problem back to the decision maker by just presenting the range of different consequences and asking him or her to give an overall assessment. (Such studies are sometimes called *cost-consequences analyses*.)

Alternatively, the various consequences could be combined in a single generic measure of health improvement. In another form of evaluation, *cost-utility analysis* (CUA), states of health are valued relative to one another through the use of health state preference values or health *utilities*. Then the superiority of one treatment over another can be expressed in terms of the quality adjusted life years (QALYs) gained (see fig 2). The use of a generic measure of outcome, such as the

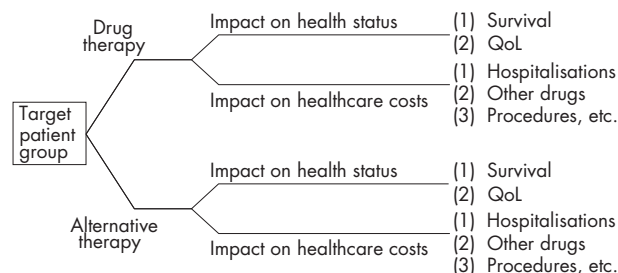


Figure 1 Basic components of economic evaluation. QoL, quality of life.

Abbreviations: CBA, cost-benefit analysis; CEA, cost-effectiveness analysis; CUA, cost-utility analysis; PABC, Pharmaceutical Benefits Advisory Committee; QALY, quality adjusted life year; TNF, tumour necrosis factor

QALY, enables us to compare the value for money of interventions in different fields of health care. The concept of the QALY is also quite useful when changes in quality of life are being traded with changes in survival. For example, a new cancer drug may be more toxic than existing therapy, thereby reducing the patient's quality of life during treatment, but may produce gains in additional survival.

Finally, in a *cost-benefit analysis* (CBA), the various consequences may be valued, relative to one another, in monetary terms. In principle, CBA is the broadest form of economic evaluation, since all costs and consequences are expressed in the same unit (that is, money). Therefore we can assess whether the total costs of an intervention are justified by its total benefits. This contrasts with CEA and CUA, where the assessment of value for money requires some judgement of what the unit of benefit (for example, a life year or QALY) is worth to society.

WHO IS ASKING FOR PHARMACOECONOMICS STUDIES?

Australia was the first jurisdiction to use pharmacoeconomics studies as part of decision making processes for new drugs. Since 1993, economic analysis has been a requirement in the information submitted by manufacturers to the Pharmaceutical Benefits Advisory Committee (PBAC), the body that advises ministers on whether new drugs go on the national formulary, the Pharmaceutical Benefits Schedule (PBS). Listing on the PBS ensures that the drug will be reimbursed in the Australian healthcare system.²

Following Australia's lead, several other jurisdictions, including Canada, New Zealand, Norway, Finland, Sweden,

and Scotland (in the UK) request economic data as part of their formal decision making procedures for new drugs. In these jurisdictions all drugs, or all drugs used outside public hospitals, are included and in most cases the decision relates to reimbursement, as in Australia. In Scotland all drugs with a licence are reimbursed, but the Scottish medicines consortium issues guidance on their use under the National Health Service (NHS). In some cases the guidance is against use of the drug at all, or for restricted use, for a range of indications narrower than those mentioned in the licence.

In several other jurisdictions, including England, Germany, Hungary, the Netherlands, and Portugal, pharmacoeconomics studies are used, but only for selected new drugs. For example, in the Netherlands, a pharmacoeconomics study is requested only in situations where the manufacturer argues that the drug should not be clustered with existing drugs under the reference pricing scheme. (Under reference pricing, all drugs in the same cluster are given the same level of reimbursement, so if the manufacturer sets a premium price this results in a higher level of co-payment by the patient.)

Alternatively in England, the National Institute for Health and Clinical Excellence (NICE) only requests an economic study if the new drug is likely to have a major impact on the NHS, either because it represents a "breakthrough" in therapy, or because it has a much higher acquisition cost than existing medications for a given medical condition. Whether it is better to have a comprehensive or selective use of economic analysis is still a matter of debate.³

Finally, in several jurisdictions pharmacoeconomics analyses are not formally required, but are used by manufacturers and decision makers on a voluntary basis. For example, in the USA, if managed care groups request economic data, these can be supplied by manufacturers according to a format devised by the Academy of Managed Care Pharmacy.⁴ Voluntary use of economic analysis also takes place in Denmark, France, and Italy. Whether there will ever be a formal requirement in these jurisdictions is currently uncertain, but the general trend is for more jurisdictions to use economic analysis rather than fewer.⁵

In jurisdictions where pharmacoeconomics studies are formally required, the authorities usually issue a specification, or set of guidelines, for the submission of data. The existing published guidelines are broadly similar, but do differ in the detail.⁶ A good example of a recent set of guidelines is the "reference case" developed by NICE in the UK.⁷ This gives advice on the therapeutic strategies to be confirmed, the perspective for costing, the measurement and valuation of health outcomes, and the characterisation of uncertainty. There have also been attempts by researchers to standardise economic evaluation methods. In the field of musculoskeletal diseases, the organisation for measurement in rheumatology clinical trials (Outcome Measures in Rheumatology (OMERACT)) has developed a reference case for economic studies in rheumatoid arthritis.⁸ The advantage of following the reference case, where one exists, is that the results of different studies can be more reliably compared. However, since the adoption of the OMERACT reference case is entirely voluntary, the uptake has been variable. Other studies show that even when guidelines for economic evaluation are prescribed by decision makers, they are not always followed.⁹

The other major issue arising from the formal use of pharmacoeconomics is that of deciding on what constitutes good value for money. More specifically, do decision makers have a threshold value, or maximum willingness-to-pay, for a unit of health improvement (such as a QALY)? In the UK, decision makers from NICE have suggested that the important range for decision making is in the region of

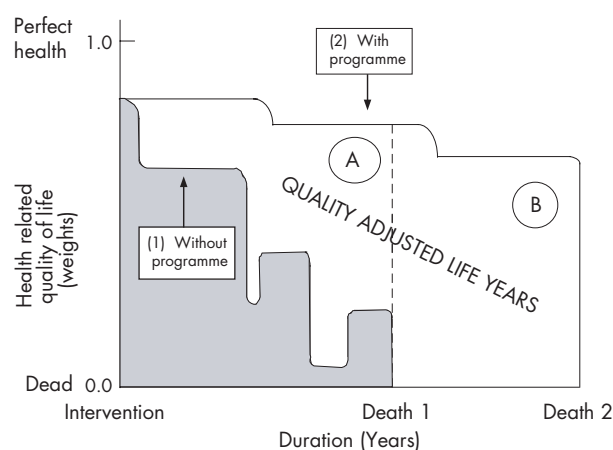


Figure 2 Quality adjusted life years (QALYs) gained from an intervention. In the conventional approach to QALYs the quality-adjustment weight for each health state is multiplied by the time in the state and then summed to calculate the number of QALYs. The advantage of the QALY as a measure of health output is that it can simultaneously capture gains from reduced morbidity (quality gains) and reduced mortality (quantity gains), and integrate these into a single measure. A simple example is displayed in the figure, in which outcomes are assumed to occur with certainty. Without the health intervention an individual's health-related quality of life would deteriorate according to the lower curve and the individual would die at time Death 1. With the health intervention the individual would deteriorate more slowly, live longer, and die at time Death 2. The area between the two curves is the number of QALYs gained by the intervention. For instruction purposes the area can be divided into two parts, A and B, as shown. Then part A is the amount of QALY gained due to quality improvements (that is, the quality gain during the time that the person would have otherwise been alive anyhow), and part B is the amount of QALY gained due to quantity improvements (that is, the amount of life extension, but adjusted by the quality of that life extension). Redrawn from Drummond MF, *et al.* Oxford: Oxford University Press, 2005, with permission.¹

£20 000–30 000 per QALY.¹⁰ This has been confirmed by empirical studies of decisions made by NICE.¹¹

Table 1 shows the results of one such empirical study of 26 decisions on new drugs, made by the PBAC in Australia.¹² It can be seen that if the incremental cost per life year gained is less than AUS \$40 000, the Committee's decision is highly likely to be positive, whereas above AUS \$80 000 it is highly likely to be negative (for example, rejection or list only if the manufacturer is willing to lower the price of the new drug).

The other interesting point about table 1 is that while the PBAC decision is largely related to the incremental cost-effectiveness ratio, there are several outliers. Several possible explanations have been offered for this. Firstly, although the results in table 1 are presented as point estimates, there may be differing amounts of uncertainty associated with each of the estimates. Secondly, the Committee may be more likely to recommend listing if the drug concerned is the only therapy available for a given group of patients, or if their health condition is very serious. Thirdly, the Committee may be more likely to list if, in the absence of listing, the cost falling on patient is very high. Finally, the Committee may be less likely to list if, despite a favourable cost-effectiveness ratio, the overall budgetary impact is likely to be large (because of the size of the patient population) or if the drug is for a disease partly determined by lifestyle (for example, obesity).

HOW DO THE NEWER DRUGS FARE IN PHARMACOECONOMICS STUDIES?

The anti-TNFs have been widely studied from an economic perspective, both in rheumatoid arthritis and other indications. For example, in a CUA based on the ATTRACT study, Kobelt *et al*¹³ found that infliximab had an incremental cost per QALY of £34 800 for two years' treatment, or £29 900 per QALY if productivity gains were included. This result is close to the threshold, of around £30 000 (or €55 000) per QALY,

set by NICE and other reimbursement bodies. Bansback *et al*¹⁴ produced cost-effectiveness estimates for three different antitumour necrosis factor (TNF) drugs in Sweden and, whereas these differed slightly, they were all around, or below, the threshold of €50 000 per QALY. This suggests that in many jurisdictions, the cost effectiveness of the anti-TNFs for rheumatoid arthritis is close to the limits of what decision makers are willing to pay.

In a paper comparing several economic models of infliximab, Drummond *et al*¹⁵ point out that the estimates produced are very sensitive to the assumptions made. Particularly important assumptions are those about the position of the anti-TNF in the sequence of therapies, the maintenance of clinical effects in the long term and the implications, for the patient, of withdrawal from therapy. These methodological uncertainties make it difficult to compare the results of economic studies assessing different drugs. They also emphasise that the reliability of cost-effectiveness estimates could be greatly improved by the use of long term data on clinical efficacy. These data could come from trials, or more likely from observational studies such as the UK biologicals registry.

Data are now beginning to emerge on the cost-effectiveness of anti-TNFs in other indications. For example, Kobelt *et al*¹⁶ found that infliximab for the treatment of ankylosing spondylitis in the UK was £35 400 per QALY if a societal perspective was considered and £73 000 per QALY if only healthcare costs were included. However, the results varied widely depending upon the assumptions made.

PHARMACOECONOMICS: FRIEND OR FOE?

There's no doubt that pharmacoeconomics represents another obstacle to the availability of new medicines. In jurisdictions using pharmacoeconomics, once a drug obtains a licence, or approval to market, a dossier must be submitted to a separate committee that will decide on reimbursement. Indeed, this process is often referred to as the "fourth hurdle", as cost effectiveness is being added to the three traditional criteria for licensing: efficacy, safety, and quality of manufacture. Often the indications for reimbursement, or guidance for use, will be narrower than the licensed indications. For example, in England and Wales, NICE ruled that cyclo-oxygenase-2 selective inhibitors should *not* be used routinely in patients with rheumatoid or osteoarthritis, but should be reserved for those patients who are at high risk of developing serious gastrointestinal adverse effects.¹⁷

In the case of anti-TNFs for rheumatoid arthritis, the restrictions imposed usually relate to the position, in the sequence of therapies, that the drugs are used. For example, it is quite common to see a requirement that, prior to the use of an anti-TNF, the patient should have previously failed two disease modifying antirheumatic drugs, including methotrexate. However, in most cases the restrictions on reimbursement tend to reflect the clinical evidence on the drugs concerned, which initially related to patients on methotrexate who still have active disease. As more becomes known about the efficacy of anti-TNFs in early disease, it will be interesting to see whether the restrictions on reimbursement are relaxed.

Although the anti-TNFs are reimbursed in most jurisdictions for rheumatoid arthritis, albeit with restrictions, they are not universally reimbursed in other indications, such as Crohn's disease, psoriatic arthritis, and psoriasis. To the extent to which such decisions have been influenced by the economic evidence, pharmacoeconomics could be said to have contributed to the non-availability of some medicines for some patients. It may also contribute to the lack of medicines in the future, to the extent that funds for research and development are limited by the lower income to companies from the sales of anti-TNFs.

Table 1 Incremental cost per additional life year gained—league table

No.	Incremental cost per additional life year gained at 1998/1999 prices (AUS\$)	PBAC decision
1	5 517	Recommended at price
2	8 374	Recommended at price
3	8 740	Recommended at price
4	17 387	Recommended at price
5	18 762	Recommended at price
6	18 983	Recommended at price
7	19 807	Recommended at lower price
8	22 255	Recommended at price
9	26 800	Recommended at price
10	38 237	Recommended at price
11	39 821	Recommended at price
12	42 697	Reject
13	43 550	Reject
14	43 550	Defer
15	43 550	Recommended at price
16	56 175	Reject
17	57 901	Recommended at price
18	63 703	Reject
19	71 582	Recommended at price
20	75 286	Recommended at price
21	85 385	Recommended at lower price
22	88 865	Reject
23	98 323	Reject
24	229 064	Recommended at lower price
25	231 650	Reject
26	256 950	Reject

AUS\$, Australian dollars. The average interbank exchange rate to US dollars for 1998/1999 was 0.63772 (range 0.68760 to 0.54850). PBAC, Pharmaceutical Benefits Advisory Committee. Published with permission from George B, *et al. Pharmacoeconomics* 2001; 19: 1103–9.¹²

On the other hand, the requirement to undertake pharmacoeconomics studies at least gives manufacturers the opportunity to demonstrate the cost effectiveness of their products. It is worth noting that many of those jurisdictions currently using pharmacoeconomics have always imposed some limitations on the reimbursement of new medicines. It is by no means certain that the use of pharmacoeconomics makes these restrictions tougher. In addition, even in jurisdictions with no apparent restrictions on the availability of new medicines, covert rationing takes place because of financial considerations. In the UK this is called "postcode rationing" as patients in one location can gain access to expensive new drugs whereas in another they cannot, because of the view decision makers take on the budgetary impact. Indeed, in the UK the existence of postcode rationing was one of the prime motivations for establishing NICE, although the Institute has not been totally successful in eliminating it.

An alternative view of pharmacoeconomics is that, rather than limiting expenditure on drugs, it directs funds to those patients who will benefit the most from new medications. It is generally true that, on an aggregate level, expenditure on drugs is not falling in the richest European countries.¹⁸ Therefore, in a world where reimbursement is driven by value for money considerations, the successful manufacturers will be those who focus on developing products that are cost effective in a wide range of indications and patients. Indeed, value for money considerations should be one of the main factors driving the drug development process. Such a shift in research priorities, rather than being a bad thing, could be beneficial to patients, their physicians, and society at large.

CONCLUSIONS

Therefore, depending on one's perspective on the issues raised above, pharmacoeconomics could be considered to be both a friend and a foe. However, the trend appears to be that more jurisdictions, rather than fewer, are using economic analysis as part of their decision making procedures. Thus, it is important that those developing, or seeking to use, expensive new medicines understand pharmacoeconomics methods and how these can be used to demonstrate value for money.

Competing interests: none declared

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REFERENCES

- 1 Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*, 3rd edn., Oxford: Oxford University Press, 2005.
- 2 Commonwealth of Australia. *Guidelines for the Pharmaceutical Industry on Preparation of Submissions to the Pharmaceutical Benefits Advisory Committee: including Economic Analyses*. Canberra: Department of Health and Community Services, 1995.
- 3 Cairns J. Providing guidance to the NHS: the Scottish Medicines Consortium and the National Institute for Clinical Excellence compared. *Health Policy* 2006;**76**:134–43.
- 4 Academy of Managed Care Pharmacy. *The AMCP Format for Formulary Submissions. Version 2.1*. Alexandria VA: AMCP, April, 2005.
- 5 Drummond MF. Economic evaluation in health care: is it really useful or are we just kidding ourselves? *Aust Econ Rev* 2004;**37**:183–97.
- 6 Hjelmgren J, Berggren F, Andersson F. Health economic guidelines—similarities, differences and some implications. *Value Health* 2001;**4**:225–50.
- 7 National Institute for Health and Clinical Excellence. *Guide to the Methods of Technology Appraisal*. London: NICE, 2004.
- 8 Maetzel A, Tugwell P, Boers M, Guillemin F, Coyle D, Drummond M, et al. Economic evaluation of programs or interventions in the management of rheumatoid arthritis: defining a consensus-based reference case. *J Rheumatol* 2003;**30**:891–6.
- 9 Anis AH, Gagnon Y. Using economic evaluations to make formulary coverage decisions: so much for guidelines. *Pharmacoeconomics* 2000;**18**:55–62.
- 10 Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ* 2004;**329**:224–7.
- 11 Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Econ* 2004;**13**:437–52.
- 12 George B, Harris A, Mitchell A. Cost-effectiveness analysis and the consistency of decision-making: evidence from pharmaceutical reimbursement in Australia (1991 to 1996). *Pharmacoeconomics* 2001;**19**:1103–9.
- 13 Kobelt G, Jönsson L, Young A, Eberhardt K. The cost-effectiveness of infliximab (Remicade) in the treatment of rheumatoid arthritis in Sweden and the United Kingdom based on the ATTRACT study. *Rheumatology* 2003;**42**:326–35.
- 14 Bansback N, Brennan A, Ghatnekar O. The cost-effectiveness of adalimumab in the treatment of moderate to severe rheumatoid arthritis patients in Sweden. *Ann Rheum Dis* 2005;**64**:995–1002.
- 15 Drummond MF, Barbieri M, Wong JB. Analytic choices in economic models of treatments for rheumatoid arthritis: what makes a difference? *Med Decis Making* 2005;**25**:520–33.
- 16 Kobelt G, Andlin-Sobocki P, Brophy S, Jonsson L, Calin A, Braun J. The burden of ankylosing spondylitis and the cost-effectiveness of treatment with infliximab (Remicade). *Rheumatology* 2004;**43**:1158–66.
- 17 National Institute for Health and Clinical Excellence. *Osteoarthritis and Rheumatoid Arthritis—coxII Inhibitors*, Technology Appraisal No.27. London: NICE, July, 2001.
- 18 Garrison L, Towse A. The drug budget silo mentality in Europe: an overview. *Value Health* 2003;**6**(suppl 1):S1–9.